

Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application.

Listing of Claims:

1. (Withdrawn) A radiolabeled immunotoxin comprising a toxic domain, a targeting domain, and at least one radionuclide atom, wherein the targeting domain is a single-chain Fv (sFv) antibody fragment that binds to a target molecule on a target cell, wherein the target molecule is not an ϵ chain of a T cell CD3 complex.
2. (Withdrawn) The radiolabeled immunotoxin of claim 1, wherein the toxic domain is a toxic polypeptide selected from the group consisting of: (a) ricin, (b) *Pseudomonas* exotoxin (PE); (c) bryodin; (d) gelonin; (e) α -sarcin; (f) aspergillin; (g) restrictocin; (h) angiogenin; (i) saporin; (j) abrin; (k) pokeweed antiviral protein (PAP); (l) a ribonuclease; (m) a pro-apoptotic polypeptide; and (n) a functional fragment of any of (a)-(m).
3. (Withdrawn) The radiolabeled immunotoxin of claim 1, wherein the toxic domain is diphtheria toxin (DT) or a functional fragment thereof.
4. (Withdrawn) The radiolabeled immunotoxin of claim 3, wherein the toxic domain comprises amino acids 1-389 of DT.
5. (Withdrawn) The radiolabeled immunotoxin of claim 1, wherein the target cell is a cancer cell.
6. (Withdrawn) The radiolabeled immunotoxin of claim 5, wherein the cancer cell is selected from the group consisting of a neural tissue cancer cell, a melanoma cell, a breast cancer cell, a lung cancer cell, a gastrointestinal cancer cell, an ovarian cancer cell, a testicular cancer

cell, a lung cancer cell, a prostate cancer cell, a cervical cancer cell, a bladder cancer cell, a vaginal cancer cell, a liver cancer cell, a renal cancer cell, a bone cancer cell, and a vascular tissue cancer cell.

7. (Withdrawn) The radiolabeled immunotoxin of claim 5, wherein the target molecule is Her-2/neu.

8. (Withdrawn) The radiolabeled immunotoxin of claim 5, wherein the target molecule is selected from the group consisting of a mucin molecule, carcinoembryonic antigen (CEA), prostate-specific antigen (PSA), folate binding receptor, A33 alpha fetoprotein, CA-125 glycoprotein, colon-specific antigen p, ferritin, p-glycoprotein, G250, OA3, PEM glycoprotein, L6 antigen, 19-9, P97, placental alkaline phosphatase, 7E11-C5, 17-1A, TAG-72, 40 kDa glycoprotein, URO-8, a tyrosinase, an interleukin- (IL-)2 receptor polypeptide, an IL-3 receptor polypeptide, an IL-13 receptor polypeptide, an IL-4 receptor polypeptide, a vascular endothelial growth factor (VEGF) receptor, a granulocyte macrophage-colony stimulating factor (GM-CSF) receptor polypeptide, an epidermal growth factor (EGF) receptor polypeptide, an insulin receptor polypeptide, an insulin-like growth factor receptor polypeptide, transferrin receptor, estrogen receptor, a T cell receptor (TCR) α -chain, a TCR β -chain, a CD4 polypeptide, a CD8 polypeptide, a CD7 polypeptide, a B cell immunoglobulin (Ig) heavy chain, a B cell Ig light chain, a CD19 polypeptide, a CD20 polypeptide, a CD22 polypeptide, a MAGE polypeptide, a BAGE polypeptide, a GAGE polypeptide, a RAGE polypeptide, a PRAME polypeptide, and a GnTV polypeptide.

9. (Withdrawn) The radiolabeled immunotoxin of claim 1, wherein the radionuclide is selected from the group consisting of ^{90}Y , ^{186}Re , ^{188}Re , ^{64}Cu , ^{67}Cu , ^{212}Pb , ^{212}Bi , ^{213}Bi , ^{123}I , ^{125}I , ^{131}I , ^{211}At , ^{32}P , ^{177}Lu , ^{47}Sc , ^{105}Rh , ^{109}Pd , ^{153}Sm , ^{199}Au , $^{99\text{m}}\text{Tc}$, ^{111}In , ^{124}I , ^{18}F , ^{11}C , ^{198}Au , ^{75}Br , ^{76}Br , ^{77}Br , ^{13}N , $^{34\text{m}}\text{Cl}$, ^{38}Cl , $^{52\text{m}}\text{Mn}$, ^{55}Co , ^{62}Cu , ^{68}Ga , ^{72}As , ^{76}As , ^{72}Se , ^{73}Se , and ^{75}Se .

10. (Withdrawn) A radiolabeled multimeric immunotoxin comprising:
(a) at least two monomers; and
(b) at least one radionuclide atom,
wherein each monomer comprises a targeting domain and a toxic domain and is physically associated with the other monomers,
wherein the targeting domain binds to a target molecule on a target cell.
11. (Withdrawn) The radiolabeled multimeric immunotoxin of claim 10, wherein each of said monomers further comprises one or more coupling moieties and the physical association of the monomer is by at least one of the one or more coupling moieties.
12. (Withdrawn) The radiolabeled multimeric immunotoxin of claim 11, wherein the coupling moiety is a terminal moiety.
13. (Withdrawn) The radiolabeled multimeric immunotoxin of claim 12, wherein the terminal moiety is a C-terminal moiety.
14. (Withdrawn) The radiolabeled multimeric immunotoxin of claim 11, wherein the one or more coupling moieties are cysteine residue.
15. (Withdrawn) The radiolabeled multimeric immunotoxin of claim 11, wherein at least one of the one or more coupling moieties is a heterologous coupling moiety.
16. (Withdrawn) The radiolabeled multimeric immunotoxin of claim 10, wherein each of the monomers comprises the same amino acid sequence.

17. (Withdrawn) An *in vitro* method of killing a target cell, the method comprising culturing the target cell with the radiolabeled immunotoxin of claim 1.

18. (Currently amended) A method comprising:

(a) identifying a subject suspected of having a ~~pathogenic cell disease~~ cancer and
(b) administering to the subject a radiolabeled immunotoxin comprising a toxic domain, a targeting domain, and at least one radionuclide atom, wherein the targeting domain is a sFv antibody fragment that binds to a target molecule on a ~~target~~ cancer cell in the subject.

19. (Withdrawn) The method of claim 18, wherein the toxic domain is a toxic polypeptide selected from the group consisting of: (a) ricin, (b) *Pseudomonas* exotoxin (PE); (c) bryodin; (d) gelonin; (e) α -sarcin; (f) aspergillin; (g) restrictocin; (h) angiogenin; (i) saporin; (j) abrin; (k) pokeweed antiviral protein (PAP); (l) a ribonuclease; (m) a pro-apoptotic polypeptide, and (n) a functional fragment of any of (a)-(m).

20. (Original) The method of claim 18, wherein the toxic domain is diphtheria toxin (DT) or a functional fragment thereof.

21. (Original) The method of claim 20, wherein the functional fragment comprises amino acids 1-389 of DT.

22. (Cancelled)

23. (Currently amended) The method of claim ~~[[22]]~~ 18, wherein the cancer cell is selected from the group consisting of a neural tissue cancer cell, a melanoma cell, a breast cancer cell, a lung cancer cell, a gastrointestinal cancer cell, an ovarian cancer cell, a testicular cancer cell, a lung cancer cell, a prostate cancer cell, a cervical cancer cell, a bladder cancer cell, a

vaginal cancer cell, a liver cancer cell, a renal cancer cell, a bone cancer cell, and a vascular tissue cancer cell.

24. (Original) The method of claim 22, wherein the target molecule is Her-2/neu.

25. (Withdrawn) The method of claim 22, wherein the target molecule is selected from the group consisting of a mucin molecule, CEA, PSA, folate binding receptor, A33 alpha fetoprotein, CA-125 glycoprotein, colon-specific antigen p, ferritin, p-glycoprotein, G250, OA3, PEM glycoprotein, L6 antigen, 19-9, P97, placental alkaline phosphatase, 7E11-C5, 17-1A, TAG-72, 40 kDa glycoprotein, URO-8, a tyrosinase, an interleukin- (IL-)2 receptor polypeptide, an IL-3 receptor polypeptide, an IL-13 receptor polypeptide, an IL-4 receptor polypeptide, a VEGF receptor, a GM-CSF receptor polypeptide, an EGF receptor polypeptide, an insulin receptor polypeptide, an insulin-like growth factor receptor polypeptide, transferrin receptor, estrogen receptor, a T cell receptor (TCR) α -chain, a TCR β -chain, a CD4 polypeptide, a CD8 polypeptide, a CD7 polypeptide, a B cell Ig heavy chain, a B cell Ig light chain, a CD19 polypeptide, a CD20 polypeptide, a CD22 polypeptide, a MAGE polypeptide, a BAGE polypeptide, a GAGE polypeptide, a RAGE polypeptide, a PRAME polypeptide, and a GnTV polypeptide.

26. (Original) The method of claim 18, wherein the method is a method of killing a target cell in the subject.

27. (Original) The method of claim 26, wherein the radionuclide is selected from the group consisting of ^{90}Y , ^{186}Re , ^{188}Re , ^{64}Cu , ^{67}Cu , ^{212}Pb , ^{212}Bi , ^{213}Bi , ^{123}I , ^{125}I , ^{131}I , ^{211}At , ^{32}P , ^{177}Lu , ^{47}Sc , ^{105}Rh , ^{109}Pd , ^{153}Sm , and ^{199}Au .

28. (Original) The method of claim 18, wherein the method is an imaging method.

29. (Original) The method of claim 28, wherein the radionuclide is selected from the group consisting of ^{186}Re , ^{188}Re , ^{64}Cu , ^{67}Cu , ^{212}Bi , ^{123}I , ^{131}I , ^{211}At , ^{177}Lu , ^{47}Sc , ^{105}Rh , ^{109}Pd , ^{153}Sm , ^{199}Au , $^{99\text{m}}\text{Tc}$, ^{111}In , ^{124}I , ^{18}F , ^{11}C , ^{198}Au , ^{75}Br , ^{76}Br , ^{77}Br , ^{13}N , $^{34\text{m}}\text{Cl}$, ^{38}Cl , $^{52\text{m}}\text{Mn}$, ^{55}Co , ^{62}Cu , ^{68}Ga , ^{72}As , ^{76}As , ^{72}Se , ^{73}Se , and ^{75}Se .

30. (Withdrawn) A method of making a radiolabeled immunotoxin, the method comprising:

(a) providing a cell comprising a vector containing a nucleic acid sequence encoding a protein, the nucleic acid sequence being operably linked to a transcriptional regulatory element (TRE);

(b) culturing the cell;

(c) extracting the protein from the culture; and

(d) attaching at least one radionuclide atom to the protein,

wherein the protein comprises a toxic domain and a targeting domain,

wherein the targeting domain is a sFv antibody fragment that binds to a target molecule on a target cell, wherein the target molecule is not a polypeptide of the CD3 complex.

31. (Withdrawn) A method of making a radiolabeled multimeric immunotoxin, the method comprising:

(a) providing one or more cells, each of the cells comprising a nucleic acid sequence encoding a monomer with a different amino acid sequence, wherein the nucleic acid sequence is operably linked to a TRE;

(b) separately culturing each of the one or more cells;

(c) extracting the monomer from each of the cultures;

(d) exposing the monomers to conditions which allow multimerization of the monomers to form a multimer comprising at least two monomers; and

(e) attaching at least one radionuclide atom to the multimer,

wherein each monomer comprises a targeting domain and a toxic domain,

wherein the targeting domain binds to a target molecule on a target cell.

32. (Withdrawn) A method of making a radiolabeled immunotoxin, the method comprising:

- (a) providing a protein comprising a toxic domain and a targeting domain; and
- (b) attaching at least one radionuclide atom to the protein,

wherein the targeting domain is a sFv antibody fragment that binds to a target molecule on a target cell, wherein the target molecule is not an ϵ chain of a T cell CD3 complex.

33. (Withdrawn) A method of making a radiolabeled multimeric immunotoxin, the method comprising:

- (a) providing a multimeric protein; and
- (b) attaching at least one radionuclide atom to the multimeric protein;

wherein the multimeric protein comprises at least two monomers,
wherein each monomer comprises a targeting domain and a toxic domain and is physically associated with the other monomers,

wherein the targeting domain binds to a target molecule on a target cell.

34. (Withdrawn) The radiolabeled multimeric immunotoxin of claim 10, wherein the targeting domain is an antibody fragment.

35. (Withdrawn) The radiolabeled multimeric immunotoxin of claim 34, wherein the antibody fragment is a sFv.

36. (Withdrawn) The radiolabeled multimeric immunotoxin of claim 34, wherein the antibody fragment binds to a target molecule on a T cell.

37. (Withdrawn) The radiolabeled multimeric immunotoxin of claim 34, wherein the target molecule is a CD3 polypeptide.

38. (Withdrawn) The radiolabeled multimeric immunotoxin of claim 10, wherein the targeting domain is a targeting polypeptide selected from the group consisting of: (a) a cytokine; (b) a ligand for a cell adhesion receptor; (c) a ligand for a signal transduction receptor; (d) a hormone; (e) a molecule that binds to a death domain family molecule; (f) an antigen; and (g) a functional fragment of any of (a) - (f).

39. (Withdrawn) The radiolabeled immunotoxin of claim 1, further comprising one or more additional targeting domains.